MAN, HIS ENVIRONMENT AND MICROBIOLOGICAL

PROBLEMS OF LONG-TERM SPACE FLIGHT

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INTRODUCTION

Man's decision to travel in outer space has challenged the ingenuity and resources of the scientific community. The field of microbiology has responded to this challenge in three broad areas as shown in table I. Many investigators in universities, industry, and the Government are developing techniques and operational procedures to meet the NASA regulation that unmanned flights to Mars be sterile (ref. 3). It is recognized that terrestrial contamination would make investigations in exobiology or the search for extraterrestrial life difficult, if not impossible.

The space science board has repeatedly and publicly pointed out the importance of the search for extraterrestrial life and in 1964 stated, "its importance and the consequences for biology justify the highest priority among all objectives in space science - indeed in the space program as a whole" (ref. 3). As the requirements for sterility and the search for extraterrestrial life involve, primarily, microscopic forms of life, it is only natural that microbiologists are deeply involved in these programs.

In the third area of endeavor, manned space flight, microbiologists are concerned with a wide spectrum of possible problems associated with placing man in a closed environment for long periods of time. Progress is being made in many areas toward the goal of long-duration, manned space flight. A considerable portion of this effort is focused on the total space cabin environment including research and development on life support subsystems (ref. 19). Microbiological investigations in support of this entire program are now under way at the NASA and other institutions. This paper summarizes the current status of this research and identifies some potential problem areas; the last section outlines the research needed to fill the gaps in our knowledge.

LIFE SUPPORT REQUIREMENTS

Before man is able to explore the solar system, provisions must be made to serve his life needs - at the same time insuring his safe return to earth. It will be necessary to provide food, water, "climate control," protective clothing, and waste removal. It is apparent that for long-duration missions, stored supplies, if used, would require enormous weights. Near-earth missions can rely on resupply, but planetary missions cannot, and for such missions recycle systems are necessary. Another way of looking at the same problem is to consider man's basic intake and output requirements as shown in table II. Thus, man



consumes the equivalent of his weight in about 15 days. In only 6 months, he takes in about a ton of oxygen, food, and water. Therefore, it will be necessary to use some of man's output for developing an input. Urine appears to be one of the first wastes which will be reclaimed since it can readily be made drinkable (urine is 93 percent water). Another area which can result in conserving weight and space is to produce oxygen onboard. One way to supply a portion of oxygen is to recover it from water and/or carbon dioxide. Recovery of oxygen from water can be accomplished by electrolysis (ref. 18).

The Integrated Life Support System

Currently under investigation at the Langley Research Center in Hampton, Virginia, is a research test facility to study and test critical life support subsystems for long-duration space missions. The integrated life support system or ILSS is a cylindrical chamber with domed ends as shown in figure 1. The chamber has a diameter of 18 feet 2 inches and a height of 18 feet. The interior volume (4150 ft³) is divided into two levels to accommodate the various functional requirements of the crew. An airlock chamber is attached to the external shell of the test bed at the lower level to permit access to the test bed when the chamber is at pressures less than atmospheric. Figure 2 is an exterior view of the ILSS test facility.

The ILSS regenerative processes are shown in figure 3. In this system, water is recovered from urine, humidity condensate, and wash water using a wick evaporator concept. Oxygen is recovered through electrolysis with the hydrogen reacting with the oxygen to generate more water. The carbon from carbon dioxide is collected as a solid. In this system solid wastes are stored.

MICROBIOLOGICAL INVESTIGATIONS

During the past 5 years, a number of microbiological studies have been conducted on the effect of space flight conditions on man and experimental animals. This section summarizes these efforts and also refers to studies made in Antarctic and on nuclear submarines for a comparison with different types of closed environmental systems.

Space Environment Test Chambers

A limited number of microbiological studies has been conducted in manned space environment test chambers and some of the characteristics of these chambers are summarized in table III (refs. 4, 6, 17, 25, 28, 29, 30, and 35). The important point in this table is the wide range of test conditions and objectives. Atmospheric conditions ranged from a normal gas mixture to 100 percent oxygen and pressures from 14.7 psi to 3.5 psi; the number of test subjects varied from two to six and the longest manned test was 56 days. Further, the depth and sophistication of the microbiological studies varied from test to test. Nevertheless, a number of interesting microbiological

results emerge from these studies as shown in table IV. In three of the five tests there was clear evidence of a transfer of micro-organisms between subjects (refs. 4, 25, 28, 29, and 30). In one test, not only did a transfer take place. but it resulted in a replacement of the normal mixed flora of the nose with a pure culture of the transferred bacteria (ref. 4). These results are in marked contrast to studies conducted in Antarctic on small groups of men cut off from physical contact with other communities for long periods of time. Here it was shown that persistent carriers of Staphylococcus aureus kept their own strains, as determined by Phage typing, despite living in very close contact with each other (refs. 23, 43, and 44). On the surface, it would appear that space cabin conditions more nearly resemble the present problem in hospitals regarding the ease with which staff and patients pick up strains of staphylococci. Alterations in skin microflora occurred and space-type diets produced changes in the number and types of fecal bacteria (refs. 6, 26, 29, 35, and 36). In one chamber test involving five men for 30 days, there was a marked reduction in the number of airborne micro-organisms so much that the subjects were breathing microbiologically clean air (ref. 4). Although data were not available for examination, Soviet investigators found in a 120-day chamber test that the number of microbes per unit volume of air rose considerably (ref. 33). These differences highlight the difficulties associated with attempting to compare results between chamber tests.

Nuclear Submarines

The Naval Biological Laboratory has conducted a number of studies on respiratory infections and airborne microbiological contamination during the course of eight nuclear (polaris) submarine cruises. The epidemiological features were unique and consisted of about 110 men living in a closed environmental system for periods up to 7 weeks. As a rule, herd-infection, herd-immunity took place with infection occurring the first week and group immunity by the fourth week. One patrol, number five, followed the usual herd-infection, herd-immunity pattern, but at the sixth week they took on three new crew members and upper respiratory infections rose almost immediately. Air counts were relatively low, less than 10 bacteria per cubic foot of air and counts were related to station activity. It was the general impression that upper respiratory infections were not airborne but due to close contact (ref. 47).

On one patrol an outbreak of <u>Mycoplasma pneumoniae</u> occurred which had a long latent period of 26 days. It was assumed that the disease was contacted from the civilian population of West Scotland before the patrol commenced (ref. 39).

Space Flight Studies

Only a limited number of microbiological studies have been reported on space flights in the United States and Russia. In a recent U.S. study, Gemini crew members and flight hardware were sampled before and after flight. The data indicated a simplification of the indigenous microflora of the crews with a decrease in the type and increase in total numbers. There was evidence that

a transfer of micro-organisms between crew members took place. Samples from the flight hardware indicated a buildup of micro-organisms, but a simplification as to types was observed (ref. 48).

Studies conducted by Russian investigators before and after certain Vostok flights showed interesting immunological changes and alterations in the auto or indigenous microflora. For example, with some crew members there was an increase in lysozyme activity, a natural antibacterial substance, in the Cosmonaut's saliva during the prelaunch period. It was concluded, however, that the bactericidal properties of the body as measured on the skin and neutrophil activity were generally within normal limits. Increased neutrophil activity was noted after the flights with certain of the Cosmonauts. The autoflora of the four Cosmonauts remained more or less within normal limits during preflight training. On postflight examination, two of the astronauts had an increase in the number of throat micro-organisms, that is, approximately 10 times higher than the physiological norm. In one case, there was an increase in the number of bacteria recovered from the deeper layers of the forearm skin (ref. 1).

Experimental Studies

As shown in table V, a number of experimental studies has been conducted on the effect of space flight conditions on infectious agents and disease. This effort has produced a new term in microbiology, "parabarosis," or altered barometric pressure and atmospheric composition on susceptibility to infection. In general, these studies have shown that altitude stress lowers resistance to infection with Klebsiella pneumoniae, Pasteurella tularensis, and salmonella (refs. 5, 11, and 42) and produced larger skin lesions with Staphylococcus aureus which healed at a slower rate than mice maintained at ground level before challenge (ref. 41). On the other hand, resistance of mice to mengovirus was related to changes in experimental conditions. In other words, altitude stress per se did not influence resistance to infection, but changes from space cabin conditions to ground level and vice versa did result in increased susceptibility to the virus (ref. 13).

Giron and Schmidt (ref. 14) found that acclimatization of rabbits to normal pO₂ at 18,000 feet for 7 days was without demonstrable effect on production of antibody against vaccinia virus. Huang (ref. 16) was able to show that parabaric conditions markedly inhibited interferon production. Mice maintained either at a simulated depth of 213 feet in sea water (95 psig), or at a simulated altitude of 37,000 feet (3.1 psig) for 2 weeks showed approximately eightfold depression in the level of serum interferon compared to the control mice kept in a similar chamber but maintained at one atmosphere with air from a tank.

Russian investigators have found that dogs exposed to space flight factors exhibited a wavelike fluctuation of the phagocytic index. During the first week after flight, the phagocytic index was low. Moderate immunological changes persisted in all dogs for months and sometimes years. It was concluded that the appearance of Escherichia coli in the oral cavity in the immediate postflight period reflected a drop in the immunological activity (refs. 2 and 46).

SPACE FLIGHT FACTORS AND MICROBIOLOGICAL PROBLEMS

Before considering some of the microbiological problems which might occur in space cabins, it is worthwhile at this time to briefly review some of the factors involved in the classical epidemiology of infectious diseases. A comparison of these factors with the space cabin environment might cast some light on the types of microbial diseases to expect in space flight.

Exogenous Versus Endogenous Disease

Listed in the left-hand column of table VI are the usual modes of transmission of infectious agents: food, water, air, contact; including direct and indirect through fomites and vectors. The truly infectious type of microbial disease with an exogenous origin results from the direct outcome of exposure to the virulent pathogen by one of the modes listed in table VI. The ingestion of water contaminated with the typhoid bacillus, inhalation of air containing tuberculosis, or the bite of a mosquito harboring yellow fever are classical examples of the exogenous type of microbial disease. On the other hand, an examination of the factors peculiar to space flight listed in the right-hand column of table VI shows that at least four of the factors usually involved in exogenous microbial diseases will be missing, or at least downgraded in effectiveness. For example, even though the astronaut will drink water recovered from urine, humidity condensate, and wash water, the water will be sterile. Therefore, one can eliminate water as a source of concern in the transmission of microbes inside the space cabin. In all probability, the space-type diet will be treated in such a manner as to prevent spoilage on long missions. Such food may not be sterile, but it will probably have a low bacteria count and certainly be free of the classical foodborne pathogens such as staphylococci, shigella, and salmonella. A highly efficient circulating and filtration system including catalytic burners will tend to reduce the number of airborne micro-organisms. In addition, three other factors will have a tendency to downgrade air as a mode of transmission inside the space cabin. First, it can be assumed that during preflight isolation the astronauts will exchange upper respiratory tract micro-organisms and, in general, equilibriate in regard to a common immunity. Second, as outside individuals will not be introduced into the space cabin, there will be little chance for a new source of upper respiratory pathogens. Finally, in the absence of gravity one may anticipate that the particles normally deposited in the respiratory tract by sedimentation, principally those particles of 1-8 microns in diameter, will be exhaled again with no deposition (ref. 31).

Included in table VI (left-hand side) are a list of some factors that could alter host resistance to infection. The items in this column are by no means exhaustive. It should also be pointed out that the precise means by which these abnormal states influence the host-parasite conflict are, in most instances, understood poorly, or not at all. As will be pointed out below, two factors, indigenous or normal flora and weather, are worth considering in some detail because of their possible implications in space cabin environments.

Indigenous Flora

Strictly speaking, the normal flora cannot be classified as a host resistance mechanism since the microbes are outsiders living with but not part of the host. It is felt, however, that the flora does interfere with colonization by outside parasites since they only support a finite number of micro-organisms. There is also the possibility that the normal flora affects general host physiology by a continuous stimulation of the immune system. It is known, for instance, that alteration or elimination of the host flora can produce drastic results as seen in patients on long-duration antibiotic therapy (refs. 7 and 9).

Evidence is already available from ground-based simulator studies, experimental animals, and space flight that alterations occur in the indigenous flora. Subjects on long-term space-type diets have shown changes in the numbers and types of intestinal flora (refs. 35 and 36). It is thus becoming apparent that alterations in the indigenous or normal flora will be important on long-duration missions and this subject is discussed again in the section on "Research Needs."

Weather

It is known that many infectious diseases display a regular pattern of seasonal incidence. For example, Streptococcal pharyngitis is most frequent in early winter, and diarrhea due to coliform and other organisms prevails in the summer. These seasonal patterns are usually explained by a variety of factors such as prevalence of insect vectors, temperature, and humidity, and crowding of the host. Seasonal fluctuations may also be due at least in part to the effects of the weather on host physiology and resistance mechanisms. However, for many infectious diseases, seasonal patterns are completely unexplained (ref. 9). As the space cabin will be maintained under constant temperature and humidity one can rule out the influence of weather or seasonal variation as a factor in the epidemiology or spread of exogenous microbial diseases on long-duration missions. In addition, the obvious lack of any insect vectors inside the space cabin plus the above-mentioned factors all tend to downgrade the role of exogenous diseases on long space missions.

Endogenous Microbial Diseases

Therefore, if one accepts the concept that the truly infectious type of microbial disease with an exogenous origin will be downgraded in the space cabin environment, it would appear that the microbial diseases of endogenous origin will become important as shown in table VII. The expression endogenous microbial diseases refers to any pathological condition caused by micro-organisms acquired at some prior time which have persisted in the body as part of its indigenous microbiota. Microbial diseases caused by these types of micro-organisms include the coliform and other Gram-negative bacilli, staphylococci, and nonhemoloytic streptococci, various kinds of yeasts and fungi and probably many viruses still unidentified (ref. 7).

It is known that endogenous microbial infections can become activated by many different kinds of changes either in the host or in the environment. For

example, persons who carry the virus of herpes simplex commonly have a high level of neutralization antibodies for this virus in their serum; however, they can experience transient episodes of virus multiplication under the influence of nonspecific stimuli - as varied as certain types of fever, fatigue, exposure to the sun, or section of the trigeminal nerve. The result is then the production of herpes blisters even in the presence of humoral antibody to the virus (ref. 7).

Many other similar examples could be cited but the important point is that endogenous microbial diseases are, to a large extent, indirectly the expressions of environmental forces. Although nonspecific stresses increase the vulnerability of the host to endogenous micro-organisms, it can be cited there is little, if any, understanding of the mechanisms through which these effects are exerted.

It thus becomes clear that if one accepts the hypothesis of the role of endogenous microbial diseases in space cabin environments, it becomes equally important to understand the factors which precipitate such diseases.

Level of Effects

In addition to the major problem area of endogenous microbial diseases, which could develop on long-duration missions, space flight conditions could also be felt at different biological levels within the space cabin. For convenience, these have been divided into micro-organisms and host effects as shown in table VII. The final outcome of these effects could very well be expressed in the general problem of endogenous microbial disease.

Micro-Organism

It is well known that viruses, bacteria, and other micro-organisms can undergo mutations affecting most of their characteristics including virulence and immunologic specificity. One well-known mutagenic agent is radiation and one can assume that long-term exposure, albiet at low levels, to cosmic radiation will produce changes in both micro-organism and host population of a space cabin. What specific changes, if any, will result from such an exposure are impossible to predict at this time. One can visualize, however, a combined effect in which radiation depresses host response through the phagocytic system and at the same time selects a mutant with increased virulence. The end result could be the selection of an organism from the indigenous flora with the capability to divide in a host with a weakened defense mechanism. Although specific cause and effect relationships will be difficult to establish for such situations, it is this type of problem that one could very well encounter under long-term space flight.

Host

Reference has already been made to the possible deleterious effects of cosmic radiation on host response to infectious agents. Another factor peculiar

to space flight which could affect the astronaut's ability to cope with exogenous or endogenous infections is the overall stress imposed by long-term space missions. There is one experimental study which might cast some light on this potential problem area. In this experiment, the stress induced by taking mice from ground-level conditions to high altitudes and vice versa was sufficient to lower the animal's resistance to the mengovirus. Although more data will be needed before definitive conclusions can be reached, it is possible that space flight stress could be mediated at the cellar level. If this is the case, then the role of viruses in the precipitation of endogenous infections could be extremely important on long-duration missions. Again, cause and effect relationships will be difficult to establish, but research should be directed toward a more complete understanding of space flight stress factors on this problem.

RESEARCH NEEDS

In a science as young as space, it is not surprising that a lack of data exists on the microbiological aspects of manned flight. As a matter of fact, until man decided to explore outer space and the ocean depths, there was very little motivation or reason to study the effect of these environments on man and the associated microbiological problems. Now, as man prepares for long-duration missions, it becomes important to know that man with his micro-organisms can survive in these types of environments in order to insure his safe return to earth. Therefore, it becomes important not only to identify problem areas but also the gaps that exist in our knowledge and the research needed to fill these gaps. It should also be pointed out such programs are not only important to our space program but such information could very well be applied to a better understanding of the health and welfare of man on earth.

Table VIII lists some of the research needed in support of long-term manned space flight. It should be pointed out that these programs are based on speculations developed in the previous section and represent limited thinking; in addition, this list is far from exhaustive - other areas will also require examination and as data develop, shifts in program emphasis will take place. Finally, it should be pointed out that the research needs identified in table VIII are those which can be conducted in ground-based facilities. The study of other factors, i.e., cosmic radiation, weightlessness, and altered biorhythms, on microbiological problems of man in closed environments will have to be conducted in earth-orbiting space laboratories before interplanetary missions are attempted.

Space Cabin Environment Studies

To date, only a limited number of studies have been conducted in ground-based space cabin simulators. It is evident that more work is needed in this area before man attempts interplanetary travel. First, these studies should be of long duration and duplicate in time the length of anticipated space missions. Such studies may be a year or longer in duration. It is anticipated that many of the microbiological problems discussed in this paper will not

appear, or at least will not be major problem areas, under the conditions of short-term missions. Second, there is a need to conduct these studies under the conditions of an integrated lift support system. This means that the subjects will drink water recovered from urine or humidity condensate, consume space-type food, and breathe the space cabin atmosphere. Last, the microbiological studies must be inclusive enough to cover not only man and his total environment, but it must include all major groups of micro-organisms including viruses.

Indigenous Flora Studies

The indigenous flora or microbiota of man has been extensively studied by numerous investigators and these results have been summarized in books and reviews by Rosebury (ref. 38), Marples (ref. 24), Dubos (ref. 8), and Gall (ref. 12). Yet the exact role of the microbiota in man's health and welfare is not known. Further, it is felt that a large percentage of indigenous microorganisms cannot be identified, let alone enumerated, for lack of adequate cultural techniques. These facts plus the observations that changes occur in the indigenous flora under space cabin conditions highlight the need for extensive studies in this area. Of paramount importance to such a program will be a clear understanding of the numbers and types of micro-organisms indigenous to man under "normal" or nonspace cabin conditions. Special attention should be paid to the intestinal flora because of the close relationship between host nutrition, physiology, and intestinal micro-organisms. During this program new isolation techniques will have to be developed to insure recovery of the host microbiota.

Immune Response Studies

The possible influence of the space cabin environment upon the astronaut's immune mechanisms should be investigated. Significant alterations of the immune mechanisms may produce prejudicial effects upon normal physiological processes and, in particular, may result in increased susceptibility to infection. The following immunological studies should be conducted on astronauts before, during, and after exposure to space cabin environments: determination of total serum proteins, serum electrophoresis, serum immunoelectrophoresis, serum ultracentrifugation, and single radial immunodiffusion for quantitating of serum immunoglobulins.

Endogenous, Exogenous Microbial Diseases and Chemotherapy

If bacterial infections do occur under simulator test conditions, it will be important to determine if the casual agent is one transmitted by classical means or if the disease is endogenous in origin. Equally important, will the infection respond to accepted antibacterial therapy or will severe reactions be generated in a subject who has an altered flora as a result of the space cabin environment? Again, determining the role of the indigenous microbial flora in the ecology of space cabin environments becomes important.

Airborne Micro-Organisms

As a part of the total microbiological picture of man in a space cabin environment, it will be important to determine the numbers and types of microorganisms in the circulating air. This is particularly important in regard to alterations in the indigenous flora, the transfer of micro-organisms between subjects and the immune response. An important part of such a study will be a careful characterization of viral isolates.

Experimental "Parabaric" Studies

Although a start has been made on examining parabarosis under laboratory conditions, much more work is needed in this area. In contrast to space cabin simulator studies which are expensive to conduct and limited in number, much meaningful data can be obtained in the laboratory using small animals and scaled-down test chambers. Similar studies as those proposed for man tests should be conducted plus further examination of the effect of space flight conditions on resistance to exogenous infections.

Theoretical Studies

It is also recommended that the microbiological problems of closed systems be examined through the use of appropriate mathematical models. Although this technique has not been widely employed in biology, its usefulness in dealing with other complex multifactorial problems suggests it has a role in bioastronautics. Through this approach, a number of factors closely interrelated yet constantly changing in a somewhat predictable manner are identified. If appropriate mathematical models can be found, or developed, their fluctuations can be reduced to mathematical formulation and can thus be subjected to simultaneous study. With computer aid, the change produced by one variable present in the system or introduced at will can be compared with the change resulting from another variable. The fact that many large variables such as temperature, humidity, and diet are under control in a space cabin suggests such models may be a practical way to approach this problem. If progress could be made in this area, it would encourage the use of such models in examining the multivariable situations found in nature (refs. 7 and 15).

LIFE SUPPORT SUBSYSTEM DEVELOPMENT

Water Management

One of the most critical subsystems in any integrated life support system is water management or the recovery of potable water from urine, humidity condensate, or wash water. A number of physical-chemical approaches for water recovery are being actively pursued and the status of this effort was recently reviewed by Popma and Collins (refs. 34). Although considerable progress has been made on the engineering side of the program, there are still many unsolved microbiological problems. For example, only recently were bacteriologic

standards set for water recovery systems. Although still tentative, these standards state that the bacterial counts must not exceed 10 micro-organisms per milliliter in any part of the system. When one considers the source of the recovered water and the constraints of closed ecological systems for long-duration missions, it soon becomes apparent that public health standards would not be acceptable. The introduction of these new standards places before the microbiologist a broad set of questions which require answers. For example, what is the best method for on-line sterilization of the system? What are the on-line monitoring requirements to insure that the standards of no more than 10 micro-organisms per milliliter are being met? Also, what are the long-term effects on the person who consumes water with these standards? It is anticipated that numerous other problems will develop as work progresses in this area.

Waste Management

It is anticipated that on short-duration missions solid wastes will be stored onboard the spacecraft. For long-duration missions, viz., interplanetary travel, it will be necessary to treat and dispose of the waste in a microbiologically safe manner. A number of prototype systems for both short- and long-duration missions have been developed; to date, none of them meet all the requirements for an aesthetically acceptable and microbiologically safe system which will operate under zero-g conditions. It is obvious that the microbiologist will have to work very closely with the engineer in all phases of design, development, and testing of any waste management system.

Personal Hygiene

For a number of reasons, including psychological, it will be necessary to provide the astronaut on long-duration missions with acceptable, and microbiological safe personal hygiene measures. It may be necessary to provide full-body shower facilities, and certainly day-to-day face and hands cleansing must be acceptable and safe. Again, close working relations must be established between the engineer and microbiologist to insure that all design requirements are being met.

REFERENCES

- 1. Alekseyeva, O. G.: Some Natural Immunity Factors and Cosmonaut Autoflora During the Training Period and Following the Flights of "Vostok,"

 "Vostok 3," and "Vostok 4." NASA TT F-368, Mar. 1966, pp. 278-289.
- 2. Alekseyeva, O. G.; and Volkova, A. P.: Influence of Space-Flight Factors in the Bactericidal Activity of the Body. Problems of Space Biology, vol. 1, 1962, pp. 201-209.
- 3. Anon.: Spacecraft Sterilization Technology. NASA SP-108, 1966.
- 4. Anon.: Manned Environmental System Assessment. NASA CR-134, Nov. 1964.
- 5. Berry, L. J.: Altitude Stress: Its Effect on Tissue Citrate and Salmonellosis in Mice. Proc. Soc. Exp. Biol. and Med., vol. 95, 1957, pp. 246-249.
- 6. Cordaro, Joseph T.; Sellers, Walter M.; Ball, Robert J.; and Schmidt, Jerome P.: Study of Man During a 56-Day Exposure to an Oxygen-Helium Atmosphere at 258 mm. Hg. Total Pressure, X. Enteric Microbial Flora. Aerospace Medicine, vol. 37, no. 6, June 1966, pp. 594-596.
- 7. Dubos, René: Man Adapting. Yale University Press, 1965.
- 8. Dubos, René: The Microbiota of the Gastrointestinal Tract. Gastroenterology, vol. 51, no. 5 pt. 2, 1966, pp. 868-874.
- 9. Dubos, René; and Hirsch, J. G.: Bacterial and Mycotic Infections of Man. J. B. Lippincott Co., 1965, pp. 146-180.
- 10. Duff, Fratis L.; and Collins, Thomas A.: Spacecrew Epidemiology. Astronautics, vol. 5, no. 2, 1960, pp. 42-48.
- 11. Ehrlich, R.; and Mieszkuc, J.: Effects of Space Cabin Environment on Resistance to Infection. 1. Effect of 18,000 Foot Altitude on Resistance to Respiratory Infection. J. Infectious Diseases, vol. 110, 1962, pp. 278-281.
- 12. Gall, Lorraine S.: Study of the Normal Fecal Bacterial Flora of Man. NASA CR-467, June 1966.
- 13. Giron, D. J.; Pindak, F. F.; and Schmidt, J. P.: To be published in Aerospace Medicine.
- 14. Giron, D. J.; and Schmidt, J. P.: USAF School of Aero-space Medicine Technical Report 66-82, 1966.
- 15. Goffman, William.: A Mathematical Model For Describing the Compatibility of Infectious Diseases. J. Theoretical Biol., vol. 11, 1966, pp. 349-361.

- 16. Gordon, Francis: Effect of Parabarosis (Altered Barometric Pressure and Atmospheric Composition) on Susceptibility to Infection. Am. Soc. Microbiol., Roundtable, 67th Annual Meeting, 1967.
- 17. Hargreaves, J. J.; Robertson, W. G.; Ulvedal, Frode.; Zeft, H. J.; and Welch, B. E.: Study of Man During a 56-Day Exposure to an Oxygen-Helium Atmosphere at 258 mm. Hg. Total Pressure. I. Introduction and General Experimental Design. Aerospace Medicine, vol. 37, no. 6, June 1966, pp. 552-555.
- 18. Heitchue, R. D.: Space Age Fundamentals. Douglas Report SM-47656, Douglas Aircraft Co., Inc., 1964, p. 52.
- 19. Jones, Walton L.: Statement Before the Subcommittee on Advanced Research and Technology, Committee on Science and Astronautics, House of Representatives. Dec. 27, 1965, p. 28.
- 20. Levashov, V. V.: New Aspects of Personal Hygiene. NASA TT F-368, Mar. 1966, pp. 163-165.
- 21. Loudon, Robert G.: Airborne Transmission of Infection in Low Gravitational Fields A Brief Review. Aero-Space Medicine, Mar. 1965, pp. 230-232.
- 22. Luckey, T. D.: Potential Microbic Shock in Manned Aero-Space System. Aero-Space Medicine, vol. 37, no. 12, Dec. 1966, pp. 1223-1228.
- 23. McLean, A. L.: Bacteriological and Other Researches; Australasian Antarctic Expedition. Scientific Reports, vol. 7, pt. 4, 1919.
- 24. Marples, Mary J.: The Ecology of the Human Skin. Charles C. Thomas, 1965, pp. 596-636.
- 25. Michel, Edward L.; Smith, George B., Jr.; and Johnson, Richard S.: Gaseous Environment Considerations and Evaluation Programs Leading to Spacecraft Atmosphere Selection. NASA TN D-2506, Jan. 1965.
- 26. Microbiological Considerations Within Manned Aero-Space Systems. An Invited Session of the 66th Annual Meeting of the Am. Soc. for Microbiol., Bacteriol, Proc., 1966, pp. 7-8.
- 27. Mieszkuc, Bernard J.; and Ehrlich, Richard.: Effect of Space Cabin Environments on Resistance of Mice to Infection with Klebsiella pneumoniae. Tech. Doc. Rept., no. SAM-TDR-64-9, 1964.
- 28. Moyer, James E.: Microbiological Problems of Sealed Cabin Environments. Developments in Industrial Microbiol., vol. 5, 1964, pp. 216-223.
- 29. Moyer, James E.; Farrell, Dorothy G.; Lamb, W. L.; and Mitchell, J. L.: Study of Man During a 56-Day Exposure to an Oxygen-Helium Atmosphere at 258 mm. Hg. Total Pressure. XI. Oral, Cutaneous and Aerosol Bacteriologic Evaluation. Aero-Space Medicine, vol. 37, no. 6, June 1966, pp. 597-600.

- 30. Moyer, James E.; and Lewis, Y. Z.: Microbiologic Studies of the Two-Man Space Cabin Simulator. Interchange of Oral and Intestinal Bacteria. SAM-TDR-64-3, Mar. 1964, pp. 1-10.
- 31. Muir, D. C.: Aerosol Deposition in the Lungs of Space Travelers. Nature, Feb. 26, 1966, p. 921.
- 32. Paul, J. H.; and Freese, H. L.: An Epidemiological and Bacteriological Study of the "Common Cold" in an Isolated Arctic Community (Spitsbergen). The Am. J. of Hygiene, vol. 17, no. 3, May 1933, pp. 517-535.
- 33. Petrov, R.: Problems of Space Immunology. Joint Publications Research Service, JPRS: 3, 922, TT: 66-30365, Jan. 27, 1966, pp. 1-4.
- 34. Popma, Dan C.; and Collins, Vernon G.: Space Vehicle Water Reclamation Systems A Status Report. Chem. Engineering Progress Symposium Series, vol. 62, no. 63, 1966, pp. 1-9.
- 35. Riley, P. E.; Beard, D. B.; and Gatts, James.: Effects Real and Relative of a Space-Type Diet on the Aerobic and Anaerobic Microflora of Human Feces. Aero-Space Medicine, vol. 37, 1966, pp. 820-824.
- 36. Riely, Phyllis; and Gall, Lorraine S.: Effect of Diet and Atmosphere on Intestinal and Skin Flora. NASA CR-662, Dec. 1966.
- 37. Riely, Phyllis E.; Gieb, Donna.; and Shorenstein, Diane: Determination of the Indigenous Microflora of Men in Controlled Environments.

 AMRL-TR-66-33, April 1966.
- 38. Rosebury, Theodore: Microorganisms Indigenous to Man. The Blakiston Division, McGraw-Hill, Inc., 1962, pp. 323-324.
- 39. Sawyer, Robert; and Sommerville, Robert G.: An Outbreak of Mycoplasma pneumoniae Infection in a Nuclear Submarine. J. Amer. Med. Assoc., vol. 195, 1966, pp. 174-175.
- 40. Schmidt, Jerome P.: Influence of Intermittent 98 Percent Oxygen and 380 mm. Hg. Total Pressure on Susceptibility to Tularemia. USAF School of Aero-Space Medicine, Aero-Space Medical Division (AFSC), SAM-TR,67-9, Jan. 1967.
- 41. Schmidt, J. P.; Cordaro, J. T.; and Ball, R. J.: To be published in Applied Microbiol.
- 42. Schmidt, J. P.; Cordaro, J. T.; Busch, J.; and Ball, R. J.: USAF School of Aero-Space Medicine Tech. Rept. 67-9, 1967.
- 43. Sladen, W. J. L.: Staphylococci in Noses and Streptococci in Throats of Isolated and Semi-Isolated Antarctic Communities. J. Hyg., vol. 63, 1965, pp. 105-116.

- 44. Sladen, W. J. L.: Science in Antarctica: Part I, The Life Sciences in Antarctica, Chap. 18, Medical Microbiology. National Acad. of Sciences, National Research Council, Publication 839, 1961, pp. 151-155.
- 45. Space Science Board: Directions for the Future: Part 3, Chap. 10, Medicine and Physiology. National Acad. of Sciences, National Research Council, Feb. 1966.
- 46. Volkova, A. P.: Changes in Certain Factors of Natural Immunity of Dogs Flying in the Fourth and Fifth Satellite-Ships. Artificial Earth Satellites, vol. 15, Jan. 1964, pp. 111-115.
- 47. Watkins, H. M. S.; and Mazarella, M. A.: Epidemiological Studies Aboard a Polaris Submarine. Presented at 7th Annual Symposium, Instrumentation Show, 1965, Bethesda, Maryland.
- 48. Wheeler, H. O.; Kemmerer, W. I.; Dietlein, L. F.; and Berry, C. A.: Effects of Space Flight Upon Indigenous Microflora of Gemini Crew Members. Bacteriol. Proc., 67th Annual Meeting, 1967, p. 16.
- 49. Zhukov-Vereznikov, N. N.: Results of Microbiological and Cytological Investigations on Vostok-Type Spacecraft. NASA TT F-281, Dec. 1964.

TABLE I

ROLE OF MICROBIOLOGY IN THE SPACE PROGRAM

- SPACECRAFT STERILIZATION
 STERILE UNMANNED FLIGHTS TO MARS
- EXOBIOLOGY

 SEARCH FOR EXTRATERRESTRIAL LIFE
- MANNED FLIGHTS
 MAN IN CLOSED ENVIRONMENTS

TABLE II

MAN'S INTAKE AND OUTPUT

INTAKE	(LB/DAY)
OXYGEN	2.0
WATER	6.6
FOOD	2.0
	10.6
OUTPUT	
CARBON DIOXIDE	2.5
WATER	
PERSPIRATION AND RESPIRATION	3.3
URINE	4.0
FECES	0.4
SOLIDS (FECAL)	0.4
	10.6

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TABLE III

CHARACTERISTICS OF SPACE ENVIRONMENT TEST CHAMBERS

LOCATION OF CHAMBER	DIMENSIONS	ATMOSPHERE	NO. TEST	NO. TESTS	LENGTH OF TEST (DAYS)
			CNE		
	12 FT LONG 8 FT HIGH 5 FT WIDE	AMBIENT TO ESSENTIALLY 100 PERCENT OXYGEN, SEA LEVEL TO 33 500 FEET	2	11	14-30
AEROSPACE MEDICINE	19 FT LONG 8 FT WIDE DOUBLE WALL 3 COMPARTMENTS	OXYGEN - HELIUM 258 MM Hg TOTAL 175 MM Hg PO ₂ 74 MM Hg PH _e 1.9 MM Hg PN ₂	4	П	56
REPUBLIC AVIATION CORP.	30 FT LONG 13 FT DIAMETER 2 COMPARTMENTS	100 PERCENT OXYGEN, TOTAL PRESSURES OF: 3.8 PSI 7.4 PSI 5.0 PSI 14.7 PSI	9	4	14
A EROSPA CE MEDICA L RESEA RCH LA BORATORIES AIR FORCE SYSTEMS COMMAND	1100 CUBIC FET CONTROLLED A CTIVITY FACILITY (20 FT-20 FT)	ATMOSPHERIC 14.7 PSI 20 PERCENT 02 80 PERCENT N2	4	7	11-15 (CAF) 28-35 (CHAMBER)
THE BOEING COMPANY	2400 CUBIC FET 20 FT LONG 10 FT WIDE 8 FT HIGH	ATMOSPHERIC 14.7 PSI 20 PERCENT 02 80 PERCENT N2	ľŲ	н	30

TABLE IV. - SUMMARY OF MICROBIOLOGICAL STUDIES

SPACE ENVIRONMENT TEST CHAMBERS

- TRANSFER OF NASAL, THROAT, AND FECAL MICRO-ORGANISMS BETWEEN SUBJECTS
- ALTERATION OF SKIN MICROFLORA
- ALTERATION OF FECAL MICROFLORA
- REPLACEMENT OF NASAL AND THROAT MICROFLORA
 - REDUCTION IN NUMBER OF AIRBORNE BACTERIA

NUCLEAR SUBMARINES

- . HERD INFECTION, HERD IMMUNITY CYCLE
- PEAK OF UPPER RESPIRATORY INFECTION DURING FIRST 2 WEEKS
- OUTBREAK OF MYCOPLASMA PNEUMONIAE

SPACE FLIGHTS

U.S.

- DECREASE IN TYPES AND INCREASE IN TOTAL NUMBERS OF CREWS' INDIGENOUS FLORA
- EVIDENCE OF TRANSFER OF MICRO-ORGANISMS BETWEEN CREW MEMBERS
- · BUILD-UP OF MICRO-ORGANISMS ON FLIGHT HARDWARE

USSR

 POST-FLIGHT EXAMINATION; INCREASE IN THROAT MICRO-ORGANISMS, AND INCREASED NEUTROPHIL ACTIVITY NOTED IN CERTAIN COSMONAUTS

TABLE V

SUMMARY OF EXPERIMENTAL SPACE FLIGHT CONDITIONS ON INFECTIOUS AGENTS AND DISEASE

U.S.

- ALTITUDE STRESS REDUCED RESISTANCE TO INFECTION WITH PASTEURELLA TULARENSIS AND KLEBSIELLA PNEUMONIAE; STAPHYLOCOCCUS AUREUS PRODUCED LARGER LESIONS WHICH HEALED AT A SLOWER RATE THAN MICE AT GROUND LEVEL.
- CHANGES IN ENVIRONMENTAL CONDITIONS, THAT IS, FROM SPACE CABIN TO GROUND LEVEL AND VICE VERSA, RESULTED IN REDUCED RESISTANCE TO MENGOVIRUS.
- ALTITUDE STRESS HAD NO DEMONSTRABLE EFFECT ON ANTIBODY PRODUCTION AGAINST VACCINIA VIRUS.
- DEPRESSION OF INTERFERON PRODUCTION IN RABBITS UNDER PARABARIC CONDITIONS.

USSR

- AFTER SPACE FLIGHTS, DOGS HAD A WAVELIKE FLUCTUATION IN PHAGOCYTIC INDEX; ESCHERICHIA COLI FOUND IN ORAL CAVITY.

TABLE VI

INFECTIOUS DISEASE AND SPACE CABIN ENVIRONMENTAL FACTORS COMPARISON BETWEEN CLASSICAL EPIDEMIOLOGY OF

FACTORS INVOLVED IN THE	LOGY OF INFECTIOUS DISEASE
FACTORS I	EPIDEMIOLOGY OF

FACTORS PECULIAR TO SPACE FLIGHT WHICH COULD AFFECT THE EPIDEMIOLOGY OF INFECTIOUS DISEASES

MODES OF TRANSMISSION

F00D

WATER

AIR

CONTACT

VECTORS

SOME FACTORS THAT ALTER HOST RESISTANCE

NUTRITION

HORMONES

NORMAL FLORA

WEATHER

DI SEA SE STATE

STRESS

ALTERED GAS ATMOSPHERE

CONSTANT TEMPERATURE AND HUMIDITY

'CLEAN' AIR AND FOOD

STERILE WATER

CONFINEMENT

COSMIC RADIATION

ALTERED BIORHYTHM

WEIGHTLESSNESS

TABLE VII

EFFECTS OF LONG DURATION SPACE FLIGHT ON HOST-PARASITE RELATION*

GENERAL EFFECT

ENDOGENOUS RATHER THAN EXOGENOUS INFECTIONS

LEVEL OF EFFECT

MICRO-ORGANISM

- . GENETIC EFFECTS
- · POPULATION SELECTION
- · METABOLIC ALTERATIONS

HOST

- · PHAGOCYTIC RESPONSE
- . ANTIBODY RESPONSE
- · CELLULAR (VIRAL) SUSCEPTIBILITY

ENVIRONMENT

- · AEROSOL STABILITY
- SURFACE CONTAMINATION

^{*}REPRINTED, IN PART, FROM REF. 16.

TABLE VIII

RESEARCH NEEDS

LONG-TERM SIMULATED SPACE CABIN ENVIRONMENT STUDIES

- . INDIGENOUS FLORA STUDIES
 - · IMMUNE RESPONSE
 - . ENDOGENOUS MICROBIAL DISEASES
 - AIRBORNE MICRO-ORGANISMS
 - THERAPY

EXPERIMENTAL 'PARABARIC' STUDIES

- SUSCEPTIBILITY TO EXOGENOUS INFECTIONS
- ENDOGENOUS MICROBIAL DISEASES
- IMMUNE RESPONSE
- · INDIGENOUS FLORA
- THERAPY

THEORETICAL STUDIES

MODEL APPROACH TO MULTIFACTORIAL SYSTEMS

LIFE SUPPORT SUBSYSTEM DEVELOPMENT

- SYSTEMS
 WATER RECOVERY
 WASTE MANAGEMENT
 PERSONAL HYGIENE
- REQUIREMENTS STANDARDS ON-LINE MONITORING

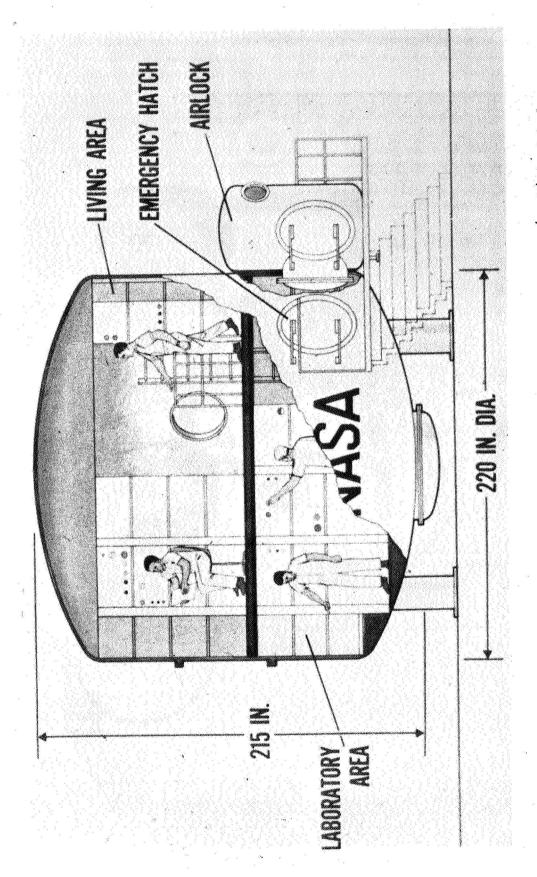


Figure 1. - Cross-section view of the Integrated Life Support System (ILSS) test bed.

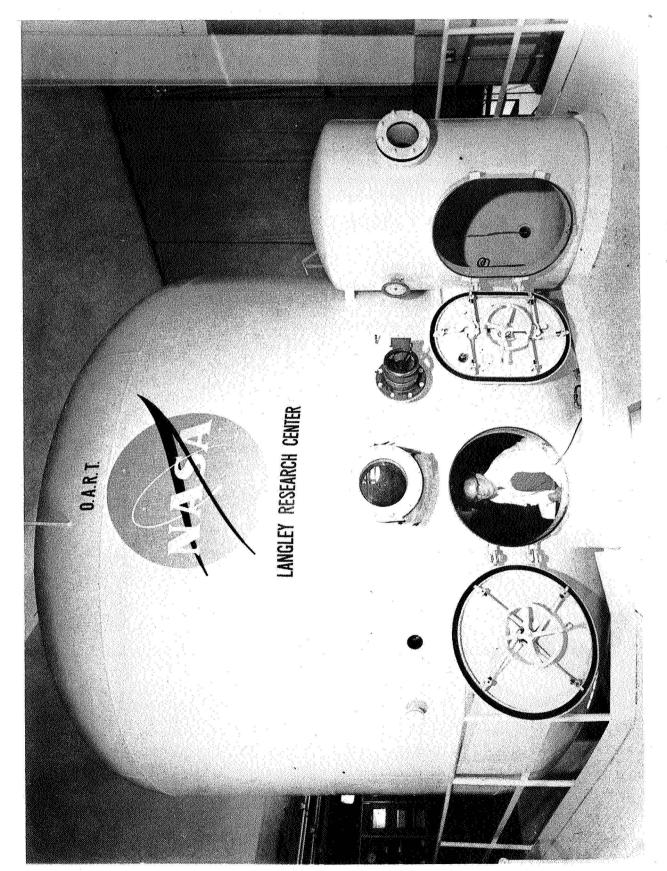


Figure 2. - Exterior view of the Integrated Life Support System (ILSS) test bed.

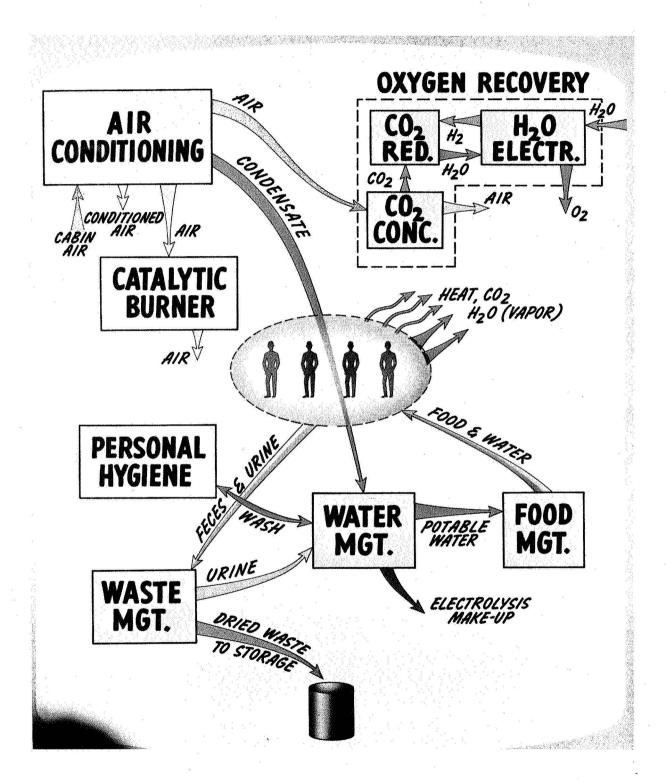


Figure 3.- Flow diagram of the Integrated Life Support System (ILSS) regenerative processes.